

chaotropes such as guanidinium (iso)thiocyanate and guanidinium hydrochloride, and urea are specifically avoided in the instant invention. As a matter of fact, the instant invention was conceived to avoid the use of harmful chemicals such as the chaotropes of Boom. The instant invention teaches the use of substantially low levels of mild lysing reagents bound to a solid support such that the biological material passes through the solid support in a flow through system that is inherently disclosed in the specification. The mixing mechanism of Boom in which an excess of chaotrope is mixed with biological material and a suspension of silica particles is completely different from the present invention in which the biological material is passed through a solid support to which a lysing reagent has been bound.

Shieh specifically teaches the use of a membrane having a pore size specific to retain red blood cells while allowing the liquid fraction of whole blood to pass through. See Shieh, Col. 10, lines 62-63. Contrary to the Examiner's assertions that Shieh teaches a method for characterizing DNA by contacting a biological material that contains DNA with a solid support . . . (See Examiner's Office Action dated June 28, 2002, page 4) Shieh does not teach isolation and subsequent characterization of DNA. Shieh teaches the lysis of red blood cells, cells that do not contain DNA. The non-ionic detergents taught by Shieh, namely Mega 8 and Triton-X are non-ionic detergents that are mild detergents that cause the rupture of cell membranes, but not nuclear membranes at the concentrations and conditions disclosed by Shieh. Thus, nuclear membranes of white blood cells containing DNA would not be lysed by the detergents at the concentrations and conditions disclosed in Shieh. Furthermore, the membrane taught by Shieh is not the membrane taught by the instant invention. Shieh specifically teaches a membrane having a pore size sufficient to retain red blood cells. Shieh teaches this limitation so that the cellular

membranes of the red blood cells can be ruptured open (leaving the nuclear membranes intact), thus releasing any glycoproteins into solution. The instant invention has no such limitation on the membrane. As a matter of fact, because the red blood cells have no DNA, there is no reason to retain the red blood cells in the instant invention. Thus, Shieh does not even provide a motivation or suggestion to lyse white blood cells to release genomic DNA. The "lysis" of red blood cells rupture the cell membrane to release glycoproteins in Shieh, is very different from the nuclear lysis of white blood cells taught by the instant invention.

Given the differences in the inventions taught by Shieh and Boom, and the different uses and goals each is used for, it would not be *prima facie* obvious to one of ordinary skill in the art to take the membrane of Shieh designed for the rupture of red blood cells using a mild, non-ionic detergent such that the glycoprotein in the cells may be measured, and assume that the method of Boom in which cells, a chaotrope and silica particles are mixed together can be modified using such a membrane to yield DNA from all kinds of cells.

Item 7. The Examiner states that "[c]laims 1-20, 24-33, 37-41, 44-49, 54-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000)."

It is respectfully pointed out to the Examiner in the prior response dated May 22, 2001 that Deggerdal teaches a method in which DNA isolation methods incorporate a limitation of using magnetic beads which comprises simultaneous steps of adding the solid support (magnetic Dynabeads) to the lysing reagent to form a suspension in which the lysing reagent is present in excess. The instant invention, on the other hand, recites the use of a solid support to which the

lysing reagent is bound and any excess lysing reagent removed. The instant invention also teaches the use of a solid support to which a lysing reagent is bound and dried before applying the biological material to be lysed. Thus, the instant invention is not the invention of Deggerdal.

The aforementioned discussion in Item 6, serves to show that the invention in Shieh is not the invention taught in the instant invention. Furthermore, there would be no motivation to one skilled in the art to combine a DNA isolation method incorporating an excess of lysing reagent and magnetic beads in a mixture with the teachings of Shieh.

Item 8. The Examiner states that “[c]laims 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above, and further in view of in view of Deggerdal (WO 96/18731).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 9. The Examiner states that “[c]laims 23 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Boom (5,234,809).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Deggerdal and Shieh overcome this rejection cited by the Examiner.

Item 10. The Examiner states that “[c]laims 7, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above and further in view of Su (5,804,684).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 11. The Examiner states that “[c]laims 42-43 are rejected under 35 U.S.C. 104(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Su (5,804,684).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom, Deggerdal and Shieh overcome this rejection cited by the Examiner.

Item 12. The Examiner states that “[c]laims 22 and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-22, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039), April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Sambrook (Molecular Cloning).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom, Deggerdal and Shieh overcome this rejection cited by the Examiner.

Item 13. The Examiner states that “[c]laims 33 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Arnold (5,599,667).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom, Deggerdal and Shieh overcome this rejection cited by the Examiner.

Item 14. The Examiner states that “[c]laim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) and further in view of Arnold (5,599,6667) as applied to claim 33, 35-36 above, and further in view of Hasebe (5,151,345).”

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom, Deggerdal and Shieh overcome this rejection cited by the Examiner.

35 USC 112

Item 15. The Examiner states that “[c]laim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention."

It is respectfully pointed out to the Examiner that the suggested amendment to the claim overcomes the Examiner's rejection.

Based on the amendments and remarks above, applicants believe that all pending claims are in condition for allowance.

If the Examiner believes that a conference would be of value in expediting the prosecution of this application, the Examiner is hereby invited to telephone undersigned counsel to arrange for such a conference.

Respectfully submitted,



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APPENDIX A

54. A process for [characterizing] analyzing DNA comprising a step of isolating nucleic acids, wherein the step of isolating comprises the steps of:
- (c) contacting a biological material that contains DNA with a solid support treated with a lysing reagent wherein the solid support has not contacted the biological material at the time of treatment;
 - (d) heating the solid support;
 - (c) treating the biological material that contains DNA with a DNA purifying reagent;
 - (d) purifying the DNA from the remainder of the biological material; and
 - (e) analyzing the purified DNA;

wherein the lysing reagent is bound to the solid support; wherein the lysing reagent is bound to the solid support and dried to the solid support.